

## EXHIBIT 1



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22312-1450  
www.uspto.gov

## NOTICE OF ALLOWANCE AND FEE(S) DUE

57539 7:90 11/13/2007  
COOPER & DUNHAM LLP  
1185 AVENUE OF THE AMERICAS  
NEW YORK, NY 10036

EXAMINER	
BORGHEEST, CHRISTINA M	
ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 11/13/2007

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,625	07/02/2003	Warren D. W. Heston	41426-GC/IPW/CY	7841
TITLE OF INVENTION: PROSTATE-SPECIFIC MEMBRANE ANTIGEN AND USES THEREOF				

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$720	\$300	\$0	\$1020	02/13/2008

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

## HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER:** Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

Page 1 of 3

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

Applicants: Virginia. W. Cornish  
Serial No.: 10/705,644  
Filed: November 10, 2003  
Exhibit 1

## PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: **Mail** Mail Stop ISSUE FEE  
 Commissioner for Patents  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 or **Fax** (571)-273-2885

**INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notification.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

57539 7190 11/13/2007

COOPER & DUNHAM LLP  
 1185 AVENUE OF THE AMERICAS  
 NEW YORK, NY 10036

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

## Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,625	07/02/2003	Warren D. W. Heston	41426-GC/JPW/CY	7841

TITLE OF INVENTION: PROSTATE-SPECIFIC MEMBRANE ANTIGEN AND USES THEREOF

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$720	\$300	\$0	\$1020	02/13/2008

EXAMINER	ART UNIT	CLASS-SUBCLASS
BORGHEST, CHRISTINA M	1649	424-009440

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
- (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1	_____
2	_____
3	_____

## 3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

## 4a. The following fee(s) are submitted:

- ☐ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies \_\_\_\_\_

## 4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

## 5. Change in Entity Status (from status indicated above)

☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant, a registered attorney or agent, or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature \_\_\_\_\_

Date \_\_\_\_\_

Typed or printed name \_\_\_\_\_

Registration No. \_\_\_\_\_

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,625	07/02/2003	Warren D. W. Hoston	41426-QC/JPW/CY	7841
57530	7590	11/13/2007	EXAMINER	
COOPER & DUNHAM LLP 1185 AVENUE OF THE AMERICAS NEW YORK, NY 10036			BORGST, CHRISTINA M	
			ART UNIT	PAPER NUMBER
			1649	
DATE MAILED: 11/13/2007				

**Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)**  
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 257 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 257 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

<b>Notice of Allowability</b>	<b>Application No.</b>		<b>Applicant(s)</b>		
	10/614,625		HESTON ET AL.		
	<b>Examiner</b>		<b>Art Unit</b>		
	Christina Borgeest		1649		

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the 17 September 2007 response to the Quayle action.
2. ☒ The allowed claim(s) is/are 24.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
  1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
  - \* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
  - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

<ol style="list-style-type: none"> <li>1. <input type="checkbox"/> Notice of References Cited (PTO-892)</li> <li>2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</li> <li>3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____</li> <li>4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material</li> </ol>	<ol style="list-style-type: none"> <li>5. <input type="checkbox"/> Notice of Informal Patent Application</li> <li>6. <input type="checkbox"/> Interview Summary (PTO-413), Paper No./Mail Date _____</li> <li>7. <input type="checkbox"/> Examiner's Amendment/Comment</li> <li>8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance</li> <li>9. <input type="checkbox"/> Other _____</li> </ol>
--	---

/Elizabeth C. Kemmerer/  
 Primary Examiner, Art Unit 1646

## EXHIBIT 2

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/056,874	CORNISH, VIRGINIA W.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 23 July 2007.

2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 30, 31, 35-40, 57 and 58 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.

6) ☒ Claim(s) 30, 31, 35-40, 57, and 58 is/are rejected.

7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some \* c) ☐ None of:

- ☐ Certified copies of the priority documents have been received.
- ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
- ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-848)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 12/11/2008
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date: \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

U.S. Patent and Trademark Office  
PTOL-326 (Rev. 08-06)

Office Action Summary

Part of Paper No./Mail Date 20071012

Applicants: Virginia W. Cornish

Serial No.: 10/705,644

Filed: November 10, 2003

Application/Control Number: 10/056,874  
Art Unit: 1639

Page 2

**DETAILED ACTION*****Status of the Application***

1. The Response filed July 23, 2007 is acknowledged.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

***Status of the Claims***

3. Claims 1-40, 55 and 56 were pending. Applicants added claims 57-58 and canceled claims 1-29, 32-34, 55, and 56. In addition, claims 30, 35, 37, 38, and 39 were amended. Therefore, claims 30, 31, 35-40, 57 and 58 are currently pending and examined on the merits.

**Withdrawn Objections/Rejections**

4. The 35 U.S.C. § 112, second paragraph rejections denoted "A-E, G and H" are withdrawn in view of Applicants' amendments and/or cancellation of claims 30, 33. The rejections under 35 U.S.C. § 112, first paragraph are withdrawn in view of Applicants' amendments to claims 30 and 38. The Lin et al. rejection under 35 U.S.C. § 102 is withdrawn in view of Applicants' amendments to claims 30 and 38. All other rejections are maintained and the arguments are addressed below.

**Outstanding Objections and/or Rejections*****Claim Rejections - 35 U.S.C. 112, second paragraph***



Application/Control Number: 10/056,874

Page 3

Art Unit: 1639

5. Claims 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Withdrawn.

B. Withdrawn.

C. Withdrawn.

D. Withdrawn.

E. Withdrawn.

F. Claim 36 recites the limitation "the molecule" in line 2. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 36 and all dependent claims are rejected under 35 USC 112, second paragraph.

G. Withdrawn.

H. Withdrawn.

***Response***

6. Applicant's arguments directed to the above 35 U.S.C. 112, second paragraph rejections were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from its original version to more clearly address applicants' newly amended and/or added claims and/or newly amended arguments.

F. [1] Applicants argue, "Applicant notes that the recitation of the term "the

Application/Control Number: 10/056,874

Page 4

Art Unit: 1639

molecule" in claim 36 has correct antecedent basis in claim 30, for example, see the preamble of claim 30" (e.g., see 12/7/06 Response, page 9, paragraph 2).

This is not found persuasive for the following reasons:

[1] The Examiner respectfully disagrees. Claim 30 described many molecules including the molecule to be identified mentioned in the preamble, the screening molecule that is covalently bound to a moiety capable of selectively binding to a receptor domain in step (a), the screening molecule that is bound to the first/second protein in step (c), etc. Thus, it is unclear which molecule Applicants is referring to.

Accordingly, the 35 U.S.C. 112, second paragraph rejections cited above are hereby maintained.

#### ***Double Patenting***

7. Claims 30, 31, 36-40, 57 and 58 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 133, 135-137, 141-147 and 150-160 of U.S. Patent No. 10/705,644 (referred to herein as '644) as evidenced by Fan et al. (Fan et al. "Covalent labeling of dihydrofolate reductase and folate transport proteins by fluorescein methotrexate" Chem. Biol. Pteridines, 1989 Proc. Int. Symp. Pteridines Folid Acid Deriv., 9<sup>th</sup> (1990), Meeting Date 1989, 1162-5. Editor(s): Curtius et al. Publisher: de Gruyter, Berlin, Fed. Rep. Ger.). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Application/Control Number: 10/056,874  
Art Unit: 1639

Page 5

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986). Although the conflicting claims are not identical, they are not patentably distinct from each other because, for example, claims 30, 31, 36-50, 57 and 58 are generic (or overlap in scope) to all that is recited in claims 133, 135-137, 141-147 and 150-160 of '644. That is, claims 133, 135-137, 141-147 and 150-160 of '644 fall entirely within the scope of claim 30, 31, 36-50, 57 and 58 of the present application or, in other words, claims 30, 31, 36-50, 57 and 58 of the present application are anticipated by claims 133, 135-137, 141-147 and 150-160 of '644.

For *claims 30 and 38*, the '644 application also claims a method for identifying a molecule that binds a known target in a cell from a pool of candidate molecules (e.g., see '644 application, preamble of claims 133 and 147). In addition, the '644 application also claims method steps for forming a screening molecule by covalently bonding each molecule in the pool of candidate molecules to a substrate capable of selectively forming a covalent bond with a receptor (e.g., see claim 133(a), wherein the substrate is methotrexate moiety of an analog of methotrexate; see also claim 147(a)). Furthermore, the '644 application also claims method steps for introducing the screening molecule into a cell culture comprising cells that express a first fusion protein of a DNA-binding domain fused to a known target receptor domain against which the candidate molecule is screened (e.g., see the '644 application, claims 30(b) and 147(b); see also claims 141 and 152 wherein the DNA binding domain is disclosed as "DHFR-(DNA-binding domain)"). In addition, the '644 application discloses a second fusion protein which comprises a receptor domain capable of binding to and forming a covalent bond with the screening molecule (e.g., see claims 133(b) and 147(b)). The '644 application does not explicit

Application/Control Number: 10/056,874  
Art Unit: 1639

Page 6

state that the second fusion protein is "capable" of binding to and forming a covalent bond with the screening molecule but the Examiner contends that this limitation is inherently disclosed by the '645 application as evidenced by Fan et al. (e.g., see Fan et al., page 1162, paragraph 1 wherein methotrexate was shown as being "capable of covalently binding" to DHFR). The '644 application also discloses the use of a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein (e.g., see '644 application, claims 133(b) and 147(b)). The '644 application also discloses permitting the screening molecule to bind to the first fusion protein and to the second fusion protein, bringing the two fusion proteins (e.g., see '644 application, claims 133(c) and 147(c)). Finally, the '644 application also discloses (d)-(e) selecting the cell that expresses the reporter gene and identifying the small molecules that binds the known target receptor (e.g., see '644 application, claims 133(d)-(e) and 147(d)-(e)). The '644 application also claims a method wherein the DNA-binding domain of the first fusion protein is LexA (e.g., see '644 application, claims 142 and 152). The '644 application also claims a method wherein the transcription activation domain of the second fusion protein is B42 (e.g., see '644 application, claims 14 and 152).

For *claim 31*, the '644 application also claims cells selected from the group consisting of insect cells, yeast cells mammalian cells and their lysates (e.g., see '644 application, claims 145 and 156 wherein mammalian and yeast cells are disclosed).

For *claim 36*, the '644 application also claims a method wherein the molecule is obtained from a combinatorial library (e.g., '644 application, claims 136 and 150).

Application/Control Number: 10/056,874  
Art Unit: 1639

Page 7

For *claim 37*, the '644 application also claims repeating the method steps for competitive binding (e.g., see '644 application, claims 137 and 151).

For *claim 39*, the '644 application also claims a method wherein the unknown protein target is encoded by a DNA from the group consisting of genomicDNA, cDNA and syntheticDNA (e.g., see '644 application, claim 159).

For *claim 40*, the '644 application also claims a method wherein the ligand has a known biological function (e.g., see claim 160).

This is a provisional obviousness-type double patenting rejection.

#### ***Response***

8. Applicant's arguments directed to the above double patenting rejection were fully considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from its original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that they traverse the rejection and will consider filing a terminal disclaimer if this is the only rejection remaining in the case (e.g., see 12/7/06 Response, page 14).

This is found unpersuasive because no terminal disclaimer has been filed and no reason was given for the traversal.

Accordingly, the double patenting rejection cited above is hereby maintained.

Application/Control Number: 10/056,874  
Art Unit: 1639

Page 8

**New Rejections**

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 30, 31, 35-40, 57 and 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For claims 30 and 38, the phrase "wherein cellular expression of the reporter gene indicates that the molecule is able to bind to the known target receptor" is vague and indefinite because rather than reciting a method step of doing something, the claims state that something is already done. That is, no method step for "measuring" or "monitoring" the cellular expression of the reporter gene is set forth (e.g., compare to the previous amendment wherein a "selecting" step and an "identifying" step were set forth. Furthermore, to the extent that no "selecting" and "identifying" steps are set forth, it is also submitted that such omissions amount to a gap between the steps because a method for identifying a molecule that binds to a known target receptor could not be performed without it. See MPEP § 2172.01.

B. Claim 30 recites the limitation "the molecule" in the second line of step (a). There is insufficient antecedent basis for this limitation in the claim. For example, claim 30 refers to several molecules including the molecule that is being identified, the screening molecule, the target receptor molecule, etc. Therefore, claim 30 and all dependent claims are rejected under 35 USC 112, second paragraph.

Application/Control Number: 10/056,874  
Art Unit: 1639

Page 9

***Claims Rejections - 35 U.S.C. 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 30, 31, 35-40, 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

A. Claims 30 and 38 were amended in the 12/7/06 response. However, the Examiner cannot find support for "(i) a penicillin-binding-protein ("PBP") or a thymidine synthase ("TS") enzyme receptor domain capable of binding to and forming the covalent bond with the screening molecule." More specifically, the specification only provides support for covalent binding to "part" of the "screening molecule" containing the "moiety capable of selectively binding to and selectively forming a covalent bond with a receptor domain", not "any" portion of the screening molecule like "the molecule" that is to be screened against the target receptor.

B. Claim 30 and 37 were amended to remove the word "small." To the extent that Applicants' claims are no longer limited to these "small" molecules, such increased breadth represents new matter.

11. Claims 30, 31, 35-40, 57 and 58 are rejected under 35 U.S.C. 112, first paragraph, as

Application/Control Number: 10/056,874  
Art Unit: 1639

Page 10

based on a disclosure which is not enabling. Active method steps for "screening" cells with activated reporter genes are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). For example, Applicants Field of Invention reads, "This invention relates to high throughput screening of cDNA libraries." However, positive method steps for screening (i.e., formerly steps (d) and (e) in claim 1 and 20) have been removed from the claims. That is, the present claims are drawn to the introduction of a single screening molecule into a cell culture but then fail to provide method steps for detecting and analyzing the molecule after it has been introduced into the cell culture (e.g., see 35 U.S.C. § 112, second paragraph rejection below). Furthermore, Applicants' currently amended claims read on the use of only one single screening molecule, which does not enable the "high throughput" aspect of the invention.

#### Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding



Application/Control Number: 10/056,874  
Art Unit: 1639

Page 11

should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jon D. Epperson/  
Primary Examiner, AU 1639



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1459  
Alexandria, Virginia 22313-1459  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,874	01/24/2002	Virginia W. Cornish	63711-A/JFW/QJC	3162
7590		10/16/2007	EXAMINER	
John P. White		BPPERSON, JON D		
Cooper & Dunham LLP		ART UNIT		
1185 Avenue of the Americas		PAPER NUMBER		
New York, NY 10036		1639		
		MAIL DATE		
		10/16/2007		
		DELIVERY MODE		
		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

## EXHIBIT 3

<b>Office Action Summary</b>	Application No.		Applicant(s)	
	10/512,497		ALTHOFF ET AL	
	Examiner		Art Unit	
	Mark Navarro		1645	

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.138(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☐ Responsive to communication(s) filed on \_\_\_\_.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 1-29, 77-80, 83 and 84 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_ is/are allowed.

6) ☒ Claim(s) 1-29, 77-80, 83 and 84 is/are rejected.

7) ☐ Claim(s) \_\_\_\_ is/are objected to.

8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date multiple

4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_

5) ☐ Notice of Informal Patent Application

6) ☐ Other: \_\_\_\_

Application/Control Number: 10/512,497  
Art Unit: 1645

Page 2

### DETAILED ACTION

Applicants preliminary amendment filed October 25, 2004 has been received and entered. Claims 30-76 and 81-82 have been cancelled. Accordingly, claims 1-29, 77-80 and 83-84 are pending in the instant application.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-10, 20, and 24-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al.

The claims are directed to a transgenic bacterial cell comprising a dimeric small molecule which comprises a first moiety known to bind a first receptor domain covalently linked to a second moiety capable of binding a second receptor domain, wherein the first and second moieties are different, nucleotide sequences which upon transcription encode a first fusion protein comprising the first receptor domain, and a second fusion protein comprising the second receptor domain, and a reporter gene wherein the expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein.

Application/Control Number: 10/512,497  
Art Unit: 1645

Page 3

Liu et al (US Patent Number 5,928,868) disclose of transgenic bacterial cells containing a first expression vector, including a DNA encoding a known first target, linked to a coding sequence for a first transcriptional module for expression as a first hybrid protein; a second expression vector including DNA encoding a second known target, linked to a coding sequence for a second transcriptional module for expression as a second hybrid protein and a third vector including a reporter gene wherein expressing the reporter gene is conditioned on the proximity of the first and second hybrid proteins. (See claims and column 10).

2. Claims 1-10, 16-29 rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al.

The claims are directed to a transgenic bacterial cell comprising a dimeric small molecule which comprises a first moiety known to bind a first receptor domain covalently linked to a second moiety capable of binding a second receptor domain, wherein the first and second moieties are different, nucleotide sequences which upon transcription encode a first fusion protein comprising the first receptor domain, and a second fusion protein comprising the second receptor domain, and a reporter gene wherein the expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein.

Lin et al (IDS Reference Number 3, 12/18/06) disclose of transgenic bacterial cells comprising dexamethasone(DEX)-methotrexate(MTX) ligand receptor pairs, and that methotrexate and dexamthasone were linked. Lin et al further teach a

Application/Control Number: 10/512,497  
Art Unit: 1645

Page 4

heterodimeric chemical inducers of dimerization between DEX-Glucocorticoid receptor (GR) and MTX-dihydrofolate reductase (DHFR). Lin et al further disclose of a heterodimeric ligand (DEX-MTX) bridges a DNA binding protein-receptor chimera (LexA-DHFR) and transcription activation protein-receptor chimera (B42-GR), effectively reconstitute a transcriptional activator and stimulating transcription of lacZ reporter gene. (See pages S6-S7).

#### ***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by cancelling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

3. Claim 77 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 3 of prior U.S. Patent No. 7,083,918. This is a double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

Application/Control Number: 10/512,497  
Art Unit: 1645

Page 5

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-29, 78-80, and 83-84 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 3 of U.S. Patent No. 7,083,918. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed transgenic bacterial cell species of methotrexate and DHFR is fully encompassed by the instantly claimed genus of a first fusion protein and a second fusion protein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861. The examiner can normally be reached on 5/4/9.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Application/Control Number: 10/512,497  
Art Unit: 1645

Page 6

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Mark Navarro  
Primary Examiner  
September 27, 2007

RECEIVED  
CENTRAL FAX CENTER

FEB 14 2008



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/512,497	05/23/2006	Eric A Althoff	66855-A-PCT-US/JPW/MJW	2136

23432	7590	10/01/2007
COOPER & DUNHAM, LLP		
1185 AVENUE OF THE AMERICAS		
NEW YORK, NY 10036		

EXAMINER	
NAVARRO, ALBERT MARK	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
10/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)